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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,291	01/09/2001	John R. Evans	PM 275507 PHM70635/US	5974

9629 7590 12/03/2002

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EXAMINER
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HUI, SAN MING R

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 12/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/756,291	EVANS ET AL.
	Examiner San-ming Hui	Art Unit 1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 13 September 2002.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

4) Claim(s) 24-50 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 24-50 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) All b) Some \* c) None of:  
1. Certified copies of the priority documents have been received.  
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) Notice of References Cited (PTO-892)      4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .  
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)      5) Notice of Informal Patent Application (PTO-152)  
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12.      6) Other: \_\_\_\_\_

### **DETAILED ACTION**

The amendments filed September 13, 2002 have been entered. The cancellation of claims 1-23 in the amendments filed September 13, 2002 is acknowledged. The addition of claims 24-50 in the amendments filed September 13, 2002 is acknowledged.

Claims 24 – 50 are drawn to a method of treating benign or malignant disease of the breast or reproductive tract.

The outstanding objection is withdrawn in view of the cancellation of the claims.

The IDS received September 13, 2002 ahs been considered.

#### ***Claim Objections***

Claim 32 is objected to because of the following informalities: no period at the end of the claim. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cancer and certain hormonal-dependent benign diseases of the breast and endometrial lining, does not reasonably provide enablement for other non-hormonal dependent conditions of the breast and the reproductive tract. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art
- 7) the predictability of the art, and
- 8) the breadth of the claims.

Applicant fails to set forth the criteria that define "benign disease of the breast and reproductive tract". In the instant case, only a limited number of "disease of the breast and reproductive tract" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the type or kind of disease treated. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant

claims read on all "disease of the breast and reproductive tract" which including non-hormonal-dependent medical conditions, such as yeast vaginitis, bacterial vaginitis, genital herpes, viral vaginitis, and sexual transmitted diseases, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention.

Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is not understood because it is an incomplete claim.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 24-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dukes (EP 0 346 014 from the IDS received February 1, 2002) in view of Lehmann et al. (US Patent Re. 28,690), GB 1 569 286 from the IDS received February 1, 2002 (herein after referred as '286), and Remington (Remington's Pharmaceutical Sciences, 18<sup>th</sup> ed., 1990, page 219).

Dukes teaches antiestrogen agents, including fulvestrant, are useful in treating postmenopausal symptoms such as urogenital atrophy affecting the vagina (See page 3, lines 56-page 4, line 1; also page 7, line 28-29). Dukes teaches that antiestrogen agent, including fulvestrant, may be used in a dosage of 50mg to 5g in vehicle comprising castor oil and benzyl alcohol (See page 7, line 20-24).

Dukes does not expressly teach the dosage of fulvestrant to be 45mg. Dukes does not expressly teach the employment of benzyl benzoate, in the percent amount of 60% w/v or less, or 50% w/v or less, or 45% w/v or less, 40% w/v or less, or 35% w/v or less, or 30% w/v or less, 25% w/v or less, or 10-25% w/v, or 12-18% w/v, as part of the vehicle herein. Dukes does not expressly teach the total amount of the fulvestrant-containing composition administered. Dukes does not expressly teach weight amount

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of castor oil and benzyl alcohol. Dukes does not expressly teach the employment of ethanol as part of the vehicle herein. Dukes does not expressly teach the dosage of fulvestrant to be 250mg. Dukes does not expressly teach the plasma concentration of fulvestrant herein.

Lehmann et al. teaches that benzyl benzoate and castor oil are well-known solvent useful as conventional carriers for steroids (See col. 1, line 21-26).

'286 teaches an intramuscular injection of testosterone derivative containing castor oil/benzoate in a ratio of 6:4 (See page 1, line 17).

Remington teaches that ethanol is one of the most commonly used solvents in pharmaceutical industry (See page 219).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ benzyl benzoate, ethanol, castor oil, and benzyl alcohol, in the herein claimed weight percent, with fulvestrant in the dosage herein, in a method of treating postmenopausal symptoms such as urogenital atrophy in the vagina.

One of ordinary skill in the art would have been motivated to employ benzyl benzoate, ethanol, castor oil, and benzyl alcohol, in the herein claimed weight percent, with fulvestrant, in the dosage herein, in a method of treating postmenopausal symptoms such as urogenital atrophy because fulvestrant is known to be useful in treating urogenital atrophy, a benign disease of the female reproductive tract in the vagina. Castor oil and benzyl alcohol are known to be effective as vehicle for fulvestrant. Ethanol is a commonly used pharmaceutical solvent. Benzyl benzoate is known to be effective as solvent for steroid compounds. Since fulvestrant is a

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estrogen derivative, benzyl benzoate would be reasonably expected to be useful as a solvent for fulvestrant. Therefore, combining one or more agents, which are known to be useful as commonly used solvents, such as benzyl benzoate, ethanol, castor oil, and benzyl alcohol, together and incorporated such combination with an estrogen derivatives, fulvestrant, would be reasonably expected to be useful in formulating a pharmaceutical composition. Furthermore, employing such fulvestrant-containing composition to treat urogenital atrophy in vagina would be reasonably expected to be effective. Moreover, the optimization of result effect parameters (e.g., amount of excipients, dosage range, and dosing regimens) is obvious as being within the skill of the artisan.

One of ordinary skill in the art would have been motivated to maintain the plasma concentration of fulvestrant herein because maintaining the therapeutic plasma level of the active compounds would be considered obvious as being within the purview of the skilled artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned

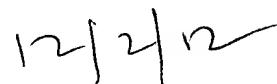
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are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui  
December 2, 2002

  
SREENI PADMANABHAN  
PRIMARY EXAMINER

  
SREENI PADMANABHAN  
PRIMARY EXAMINER